## abetalol against Alpha Methyldopa for the treatment gestational hypertention

Labetalol contra Alfa Metildopa para el tratamiento de la hipertensión gestacional

Shaimaa Abdulamer Nasir Shaimaa.abdulameer@qu.edu.iq.com https://orcid.org/0000-0002-7641-992X. Obstetric and Gynecological Department, Medical college/Al-Qadisiyah University/Iraq

Resumen

Received: 07/20/2022 Accepted: 10/19/2023 Published: 11/25/2023 DOI: http://doi.org/10.5281/zenodo.10214339

**Background**: The most frequent medical condition is hypertension. It is associated by a higher chance of adverse effects all throughout pregnancy.

**aim of study**: to match alpha methyldopa and labetalol's effectiveness in decreasing blood pressure in expectant mothers with hypertension caused by pregnancy (PIH).

**results:** Significant differences were found between the study groups referring to the typical drop in and Diastolic and Systolic blood pressure, and Comparing to the -Methyldopa group, the labetalol group required considerably less time to control blood pressure.

conclusion: A significant issue is high Bp during pregnancy. The root of all illnesses and fatalities globally. Drugs that treat hypertension play a significant role in the management of BP in mothers. In this research, we discovered that labetalol regulates diastolic and systolic function more rapidly and effectively than methyldopa. This conclusion is consistent with other observations that labetalol is efficient and ensures faster drug being used in achieving satisfactory Bp control in PIH.

**Keyword:** Labetolol, gestational hypertension, treatment methyldopa

**Antecedentes:** La condición médica más frecuente es la hipertensión. Se asocia con una mayor probabilidad de efectos adversos durante todo el embarazo.

objetivo del estudio: igualar la eficacia de la alfa metildopa y el labetalol para disminuir la presión arterial en mujeres embarazadas con hipertensión causada por el embarazo (PIH).

**Resultados:** Se encontraron diferencias significativas entre los grupos de estudio en lo que respecta a la caída típica de la presión arterial diastólica y sistólica, y en comparación con el grupo de -metildopa, el grupo de labetalol requirió considerablemente menos tiempo para controlar la presión arterial.

Conclusión: Un problema importante es la presión arterial alta durante el embarazo. La raíz de todas las enfermedades y muertes a nivel mundial. Los fármacos que tratan la hipertensión desempeñan un papel importante en el tratamiento de la PA en las madres. En esta investigación, descubrimos que el labetalol regula la función diastólica y sistólica de manera más rápida y efectiva que la metildopa. Esta conclusión es consistente con otras observaciones de que el labetalol es eficiente y garantiza un uso más rápido del fármaco para lograr un control satisfactorio de la presión arterial en la PIH.

**Palabra clave:** Labetolol, hipertensión gestacional, tratamiento con metildopa.

**Materials and methods** 

Introduction

ne of the most common pregnancy problems is the need for a caesarean section. hypertension, is a major control problem during caeserian delivery specifically. Approximately 12 to 22 percent of all pregnant women suffer from hypertensive diseases that affect their pregnancies; 70% of these are affected by prenatal HPB and 30% are affected by critical HPB1. Preeclampsia, pregnancy induced hypertention, and chronic hypertention are all high blood pressure diseases of pregnancy2. chronic HPB with superimposed preeclampsia and eclampsia are other variants of hypertensive disorders in pregnancy. unexpected deterioration in HPB may occur or appearance of endorgan symptoms like Thrombocytopenia, proteinuria, elevated liver enzyme levels, pulmonary edoema, and renal impairment, or signs such as headache or ache in the upper right quadrant. Methyldopa, alpha and beta blockers, and calcium channel blockers are the top3 drugs used to treat PIH. Research has revealed contradictory facts regarding the impacts of these drugs on the fetus and the mother throughout pregnancy. Approximately 6-8% of expectant mothers worldwide have PIH4. Methyldopa and oral labetalol are the preferred medications in the presence of hypertensive pregnancy disorders. These two medicines are easily accessible in our country. Without any adverse effects on perinatal outcomes, both drugs were discovered to be efficient in lowering blood pressure<sup>5</sup>, which lowers blood pressure and reduces peripheral conflict. Labetalol is dual alpha (α1) and beta (β1/β2) adrenergic receptor blocker with a vasodilator effect, drowsiness, and dizziness are common side effects. It works faster than methyldopa and can be given by mouth<sup>6</sup>. It is now understood that Beta-blockers penetrate the placenta and enter the fetal circulation, which might result in foetal bradycardia7. There is debate about whether

labetalol and methyldopa have antenatal side effects8.

his investigation included 120 cases attend consultation and emergency units Aldiwaniya hospital for maternity and children from June 2021 to January 2022. The staff just knows which ones to take and which ones to regulate when it comes due to PIH because it's randomly divided into either alpha methyldopa or labetalol receiving groups.

The following requirements must be met pregnant women between the ages of 20 and 40, gestational ages between 20 and 37 weeks, and women with a minimum blood pressure in systole 140 mm Hg or more. Diastolic blood pressure of 90 mmHg or greater after two BP four-hourly measurements at a previously normal BP.

Pregnant women with primary HBP who had previously taken antihypertensive medication were excluded, we exclude Pre-eclampsia and eclampsia with persistent symptoms such as headache, epigastric discomfort, and visual disturbance (fulminant eclampsia; platelet count 100 x 10 or AST >50 IU/L) (generalized tonic-clonic seizures often according to pre-eclampsia). Multiple births, placenta previa, and multiple pregnancies. pregnant women with heart, kidney, or blood problems.

working concept: At the time of admission, the following information was collected from each patient. A history of additional medical problems, such as heart disease, a previous hepatitis C infection, and certain behaviors that are medically important, such as smoking.

Clinical evaluation focuses on basic symptoms (blood pressure, body temperature, heart rate, and respiration rate), height, weight, and body mass index. Subjective evaluation of pelvic grip level.

Complete blood count (CBC) tests are performed in laboratories to determine red blood cell (RBC) counts, haemoglobin levels, white blood cell, and platelet count, urinalysis, serum creatinine, Blood urea for a kidney function test. gamma-glutamyl transferase (GGT), albumin, bilirubin, (AST and ALT), prothrombin time, and international normalized ratio (INR) are the components of the liver test profile.

Every two weeks, we do an ultrasound scan for fetal well being and Doppler ultrasound study for fetal umbilical artery<sup>9,10</sup>.

## **Procedures**

Each participant underwent the further measures associated with this study. Measurement of standard BP using a typical mercurial sphygmomanometer five to ten minutes of sitting time before taking

pressure. on left lateral position, the cuff is sized to fit the measurement of the canister arm and lies 20-30 mm above the cubital fossa, identifying the brachial artery's position relative to the rubber bladder's center and locating the upper end at heart height. Routine visits to the antenatal clinic for standard follow-up, when cases are evaluated two days after taking the drug<sup>11</sup>. If there is no decrease in blood pressure until two days after taking the drug, the dose is evaluated to control blood pressure, and the drug dose is doubled. The next two weeks, she has weekly checkups at the prenatal clinic. Then every two weeks before their birth. The mean arterial blood pressure controlled by labetalol/methyldopa, the time required for blood pressure regulation, typical drug doses required for blood pressure regulation, as well as drug side effects were noted. Every two weeks, we do an ultrasound scan for fetal well being and Doppler ultrasound study for fetal umbilical artery (Statistical analysis: Windows-based IBM-SPSS was used to evaluate the collected data. Shapiro Walk test was used to determine if the data had normal distributions. Frequency and percentage were used to enter qualitative data. Square Chi The difference between the qualitative data as determined was calculated using the two tests (2) and Fisher's test. The mean and (standard deviation) of the parametric data, as well as the mean and range of the non-parametric data, were used to depict the quantitative data. All statistical analyzes had two tails and significance levels set at P-values of 0.05 were all regarded as significant. A change is considered very significant if it occurred at P0.001, while it was considered no significant if it occurred at P > 0.05.

Table (1): Demonstrate Demographic in Current Study							
Parameter (n, %)		Labetolol (60) n=60	Methyl dopa (60)				
A	18-25	24(40%)	22(36.66 %)	0.14(ns)			
Age (years)	26-30	21(35%)	25 (41.66 %)	0.103(ns)			
	31- 40	15(25%)	13(21.66 %)	0.435(ns)			
BMI (kg/m2)	Underweight<19	3(5%)	1 (1.66%)	0.095(ns)			
	Normal =19-23	12 (20%)	10(16 %)	0.123(ns)			
(Kg/IIIZ)	Over weight >24	45 (75%)	49 (81%)	0.546(ns)			
Gravida	Primi	32(53.33%)	30 (50.0%)	0.193(ns)			
	Multi	28(%46.66)	30(50 %)	0.675(ns)			
Nonparametric Tests Chi-Square							

Categories of weight include underweight (BMI 19 kg/m2), normal weight (19–23 kg/m2), and overweight (24 kg/m2).

in the labetalol group; 20.66% had an SBP <150 mmHg, 74.37% had an SBP >150 mmHg, and a DBP <100 mmHg in 31.56%, and>100 mmHg in 68.64%, in the alpha-methyldopa group; 22.56% had an SBP <150 mmHg, 77.33% had an SBP >150 mmHg, had a DBP<100 mmHg in 26.66%, and >100 mmHg in

69.46%, Regarding BP, there was no discernible difference between the groups. Table 2.

Table 2: Before treatment, the two groups' BP distribution						
No.	Group		Labetalol (n=60)	α-Methyldopa (n=60)	P –value	
N=50	SBP	<150 mmHg	19(20.66%)	16(22.56%)	0.454(ns)	
UC=NI	SDP	>150 mmHg	41(74.37%)	44(77.33%)	0.123(ns)	
N=50	DBP	<100 mmHg	20(31.56%)	22(26.66%)	0.234(ns)	
UC=NI	DBP	>100 mmHg	40(68.64%)	38(69.46%)	0.902(ns)	
P-value						

The values in the vertical column were tested by Independent T -Test The superscript small letters (a,b) mean the same letter no difference between groups, while different letters mean a difference(A,B) between groups.

- ✓ Horizontal values were tested using a Paired-sample T test to determine the difference.
- $\checkmark$  \* Significant difference at p<0.05, \*\* highly significant less than 0.001

Regarding the mean decline in SBP and DBP, a substantial change was discovered in the group under study. Table 3

Table 3: Mean reduction in blood pressure between the 2 groups after 48 hours of therapy				
	Lab.	Ald.		
SBP	55(91.66%)	53(88.33%)		
DBP	5(8.33%)	7(11.66%)		

Regarding mean drops in SBP and DBP, there was a substantial change within the study group. table 3. -Methyldopa (n=50) and labetalol (n=50) SBP p MU (mmHg) Average Standard Deviation 5.88 2.01 3.22 1.15 4.23 DBP (mmHg) Standard deviation from the mean: 7.05 2.91 4.18 2.19 5.17 000 Table 3: Mean reduction in BP between the 2 groups after 48 hours of therapy in comparison to the group using -Methyldopa, the labetalol group required much less time to stabilize blood pressure.

Table 4: Comparing the two groups' blood pressure control times		
Labtolol		
53 patients need 2 days		
7 patients needs 5 days		
Aldomet		
45 need 6 days		
13 need 5days		
2 need 4 days		

regnancy-related high blood pressure (HBP) is the most common medical problem. Up to 10% of all pregnancies can become complicated by HBP, and this condition is associated with increased risks to the mother, newborn, and foetus such as preterm labor, antepartum haemorrhage, postpartum haemorrhage, diabetes, persistent high blood pressure, perinatal mortality, hepatic failure, or acute renal failure. Both prepartum and postoperative bleeding are common<sup>12</sup>.

The trial had 120 PIH cases that were Labetalol or alpha-methyldopa will be given at random; only the personnel was aware of which patients were on which regimen. According to a study by Subhedar *et al.*<sup>13</sup>, the majority of the 18 total instances (92 cases) happened among individuals between the ages of 15 and 24. Of them, 44 cases (48.89%) in group A and 48 instances (53.33%) were in group B, respectively. The two groups' mean ages did not differ considerably from one another. Of the 102 cases, 53 cases (58.89%) in the methyldopa group and 49 cases (54.44%) in the labetalol group were from primigravidae. The groups under study did not differ significantly from one another.

There were (52%) participants in the 21-25 year age group in a different study of Gurjar and Malewar<sup>12</sup> that found cases in that methyldopa group, compared to (51%) cases in the labetalol group. In the age range of 26 to 30 years, the methyldopa group had 47 instances (or 47%) compared to the labetalol group's 45 cases.

In this study, we report that there was no significant difference between studies in terms of the BP groups before administration in the labetalol group; 20.66% had an SBP <150 mmHg, 74.37% had a SBP >150 mmHg, and a DBP <100 mmHg in 31.56%, and>100 mmHg in 68.64%, in the alpha-methyldopa group; 22.56% had an SBP <150 mmHg, 77.33% had an SBP >150 mmHg, had a DBP<100 mmHg in 26.66%, and >100 mmHg in 69.46%, there was no significant difference between groups with respect to BP before therapy.

The average MAP in the study groups was the same as the one given earlier, according to the study by Abalos *et al*(14). MAP significantly dropped in labetalol group (p - value 0.05).

A related study, El-Qarmalawi AM *et al.* (15) found that 68.5% of individuals receiving methyldopa had a significant reduction in MAP, contrary to 15.4% of cases receiving labetalol.

The average arterial pressure of the subjects receiving methyldopa was 109.86 mmHg in the report by Subhedar *et al.*<sup>13</sup> but with labetalol, On day 7, it

decreased significantly, statistically, to 98.15 mmHg. On day 7, the average arterial pressure was 96.90 mmHg, down from the admissions average of 109.48 mmHg. It is statistically significant that MAP has decreased. On admission, MAP was comparable across the two medicines, however on day 7, a substantial drop in MAP was discovered with in labetalol group.

According to research by Pentareddy *et al.*,<sup>3</sup>, the mean systemic BP at delivery was 123.66± 10.332 in patients of methyldopa and 121.66±7.4664 in cases of labetalol. Severe hypertension was present in two patients in methyldopa group and one patient in labetalol group.

This is supported by previous study performed by Cruikshank *et al.*<sup>16</sup> who reported that in 88% of patients, labetalol promptly brought blood pressure under control. A new report by Lardoux et al., similarly 1983, found that labetalol resulted a rapid drop in blood pressure in 82% of instances, whereas Michael CA<sup>17</sup>, observed that labetalol caused a quick drop in blood pressure in 92% of cases.

Methyldopa was found to lower blood pressure from an average diastolic BP of 94.00±4.98 to 82.00±5.6 mm Hg, according to Pentareddy *et al.*,<sup>3</sup>. The mean diastolic blood pressure decreased dramatically with labetalol from 96.67±4.79 to 79.00±5.53 mmHg before and after therapy (p 0.001), and the blood pressure was significantly lower both before and after administration. The mean decrease in DBP were not noticeably different between the labetalol and methyldopa groups (p-value > 0.005).

Previously, Dharwadkar *et al.*(18) confirmed that the active anti-hypertensive drug labetalol lowered diastolic and systolic blood pressure in PIH. Only 22.5% of labetalol-treated patients who gave labetalol and phenobarbital injection received additional blood pressure control medications in addition to labetalol, compared to approximately 55% of methyldopa-treated patients who received nifedipine and phenobarbital. The results of the current study showed that labetalol is an effective drug for lowering blood pressure in patients compared to maintaining an ideal blood pressure level.

In addition, we discovered in the present investigation that the time frame for blood pressure management of labetalol patients was significantly shorter than that of the -methyldopa group.

This is in line with the results of the study by Subhedar *et al.*,<sup>13</sup> which found that labetolol group required 36.97 hours and methyldopa group required 42.22 hours to control blood pressure. The difference between the study groups was noteworthy as labetalol showed earlier blood pressure control compared to methyldopa.

A study by Alalfy M. *et al.*<sup>19</sup>, found that both methyldopa and labetalol reduce MAP starting at baseline, which is the BP before starting anti-hypertensive treatment and

lasting for 2 days, 1, 3, 5, 7, and 9 weeks after starting treatment, however, showed labetalol's significant change in BP, which regulates levels of diastolic and systolic blood pressure and MAP, a P incidence of 0.001 at 2 days, 1, 3, 5, 7, and 9 weeks after treatment and at the time of birth more effective management of blood pressure.

According to Subedar *et al.*<sup>13</sup>, 9 cases in methyldopa group (33.33%) experienced spontaneous labor, while 18 cases (66.67%) required induction. in labetolol group 24 cases (51.06%) had induced labour, while 23 cases (48.94%) had spontaneous labour and these values are statistically significant. This happens due to the fact that labetalol activates the ripening of the cervix.

Also Lamming *et al.,*<sup>20</sup> a confirm the results presented by El-Qarmalawi et al.<sup>15</sup>, which indicate a high rate of non induced labor started in labetolol using patients.

Birth outcomes were not different between groups, according to Easterling et al<sup>8</sup>. In each group, 190 (64% of the 295 cases on the nifedipine group), 186 (64% of the 290 female reported cases on labetalol), and 179 (61% of the cases 295 patients the methyldopa group) those percentages revealed the caesarean deliveries mainly due to failure of induction and abnormal cardiotocograghy.

the frequency of stillbirth, newborn death, and neonatal morbidity did not differ across groups. However, infants of recruited moms had a considerably higher rate of neonatal hospitalizations to the intensive care unit (ICU) in nifedipine group than labetalol group (p = 009) and methyldopa group (p = 004) mostly due to low birth weight. There were no differences in the typical length of stays in the intensive care unit (less than one day).

he largest global cause of morbidity and mortality during pregnancy is high BP. therapies that treat high BP play a role in controlling BP in the mother. In this study, we discovered that labetalol regulated diastolic and systolic BP more efficiently and decisively than methyldopa. A reliable and secure medication is labetalol, and it is faster in obtaining adequate blood pressure management in PIH.

## References

- Tanz LJ, Stuart JJ, Missmer SA, Rimm EB, Sumner JA, Vadnais MA, et al. Cardiovascular biomarkers in the years following pregnancies complicated by hypertensive disorders or delivered preterm. Pregnancy Hypertens. 2018;13:14–21.
- Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension. 2018;72(1):24–43.
- 3. Pentareddy MR, Shailendra D, Prasuna G, Subbaratnam Y, Naresh D, Katta R. Safety and efficacy of methyldopa and labetalol in controlling blood pressure in hypertensive disorders of pregnancy. Int J Basic Clin Pharmacol. 2017;6(4):942–7.
- Kalsoom S, Majeed N, Riaz M, Tariq S. Labetalol Versus Methyldopa: Comparison of Frequency of Small for Gestational Age in the Treatment of Pregnancy Induced Hypertension. J Rawalpindi Med Coll. 2018;346–9.
- Akhtar N, Hayat Z, Nazim F. COMPARISON BETWEN LABETALOL AND METHYLDOPA IN THE TREATEMNT OF PRE-ECLAMPSIA. JPMI J Postgrad Med Inst. 2018;32(1).
- Lin Y, Zhang Y, Jiang Y-N, Song W. Medication for management of pregnancy-induced hypertension. Clin Trials Degener Dis. 2018;3(2):83.
- Xu B, Bobek G, Makris A, Hennessy A. Antihypertensive methyldopa, labetalol, hydralazine, and clonidine reversed tumour necrosis factor-α inhibited endothelial nitric oxide synthase expression in endothelial-trophoblast cellular networks. Clin Exp Pharmacol Physiol. 2017;44(3):421–7.
- Easterling T, Mundle S, Bracken H, Parvekar S, Mool S, Magee LA, et al. Oral antihypertensive regimens (nifedipine retard, labetalol, and methyldopa) for management of severe hypertension in pregnancy: an open-label, randomised controlled trial. Lancet. 2019;394(10203):1011–21.
- Salomon LJ, Alfirevic Z, Da Silva Costa F, Deter RL, Figueras F, Ghi T al, et al. ISUOG Practice Guidelines: ultrasound assessment of fetal biometry and growth. Ultrasound Obstet Gynecol. 2019;53(6):715–23.
- Jezewski J, Wrobel J, Matonia A, Horoba K, Martinek R, Kupka T, et al. Is abdominal fetal electrocardiography an alternative to doppler ultrasound for FHR variability evaluation? Front Physiol. 2017;8:305.
- Ngene NC, Moodley J. Baseline check of blood pressure readings of an automated device in severe pre-eclampsia and healthy normotensive pregnancy. Pregnancy Hypertens. 2018;12:47–52.
- Gurjar BG, Malewar SS. Study of labetalol vs. methyldopa in treatment of pregnancy induced hypertension. Int J Reprod Contraception, Obstet Gynecol. 2019;8(6):2378–84.
- Subhedar V, Inamdar S, Hariharan C, Subhedar S. Comparison of efficacy of labetalol and methyldopa in patients with pregnancyinduced hypertension. Int J Reprod Contracept Obs Gynecol. 2013;2(1):27–34.
- Abalos E, Duley L, Steyn DW, Gialdini C. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane database Syst Rev. 2018;(10).
- ElQarmalawi AM, Morsy AH, Al-Fadly A, Obeid A, Hashem M. Labetalol vs. methyldopa in the treatment of pregnancy-induced

- hypertension. Int J Gynecol Obstet. 1995;49(2):125-30.
- Cruickshank DJ, Robertson AA, Campbell DM, MacGillivray I. Does labetalol influence the development of proteinuria in pregnancy hypertension? A randomised controlled study. Eur J Obstet Gynecol Reprod Biol. 1992;45(1):47-51.
- Michael CA. Use of labetalol in the treatment of severe hypertension during pregnancy. Br J Clin Pharmacol. 1979;8(S2):211S-215S.
- Dharwadkar MN, Kanakamma MK, Dharwadkar SN, Rajagopal K, Gopakumar C, Divya J. Study of methyl dopa versus labetalol in management of preeclampsia and gestational hypertension. Gynecol Obs. 2014;4(242):932-2161.
- 19. Alalfy M, E. Eltaieb, Mahmoud. Soliman. Labetalol in Comparison to Methyl Dopa in Treatment of Gestational Hypertension, A Randomized Trial. J Gynecol Res. 2018; 4(1): 101.
- Lamming GD, Symonds EB. Use of labetalol and methyldopa in pregnancy-induced hypertension. Br J Clin Pharmacol. 1979;8(S2):217S-222S.